European Medicines Agency

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QUESTIONS AND ANSWERS ON THE WITHDRAWAL OF THE APPLICATION FOR A SCIENTIFIC OPINION for GLOBORIX

Common name: ***vaccine against diphtheria, tetanus, pertussis, hepatitis B,* Haemophilus influenzae *type b and* Neisseria meningitidis *groups A and C***

On 11 October 2007, GlaxoSmithKline Biologicals s.a. officially notified the Committee for Medicinal Products for Human Use (CHMP) that it wishes to withdraw its application for a scientific opinion for Globorix, for primary immunisation of infants (during the first year of life) against diphtheria, tetanus, pertussis, hepatitis B, invasive disease caused by *Haemophilus influenzae* type b and *Neisseria meningitidis* group A and C, and for booster immunisation of young children during the second year of life.

The application for a CHMP scientific opinion for Globorix was being evaluated in co-operation with the World Health Organization (WHO)[1] because it was to be used as part of the 'Expanded Programme on Immunization'. Globorix was to be used exclusively in markets outside the European Union, primarily in sub-Saharan Africa.

What is Globorix?
Globorix is a vaccine containing parts of various bacteria and viruses that cause serious childhood illnesses, which can be life-threatening or cause long-lasting health problems.

What was Globorix expected to be used for?
Globorix was expected to be used to vaccinate infants under one year of age against diphtheria, tetanus, pertussis, hepatitis B and 'invasive' diseases caused by *Haemophilus influenzae* type b and *Neisseria meningitidis* groups A and C. It was also expected to be used as a booster in children during the second year of life who had already been vaccinated against these diseases.

Globorix contains small amounts of:
- toxoids (chemically weakened toxins) from the bacteria that cause diphtheria and tetanus;
- killed *Bordetella pertussis*, the bacteria that cause pertussis (whooping cough);
- polysaccharides (sugars) extracted from the 'capsules' that surround the bacteria *Haemophilus influenzae* type b and *Neisseria meningitidis* (group A and C). These bacteria can cause severe infections, including meningitis. The polysaccharides are chemically attached (conjugated) to tetanus toxoid as a carrier protein because this improves the response to the vaccine;
- parts of the hepatitis B virus.

How is Globorix expected to work?
Vaccines work by 'teaching' the immune system (the body's natural defences) how to defend itself against diseases. When a person is given the vaccine, the immune system recognises the parts of the bacteria and viruses contained in the vaccine as 'foreign' and makes antibodies against them. The immune system will then be able to produce antibodies more quickly when the person is naturally exposed to the bacteria or viruses. This helps to protect against the diseases caused by the bacteria and

[1] This product was being evaluated under Article 58 of Regulation (EC) No 726/2004.

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viruses. With Globorix, a second 'booster' dose was expected to improve protection against meningitis.

What documentation did the company present to support its application to the CHMP?
The company carried out 12 studies on Globorix: 10 looked at its use in primary vaccination in around 4,000 infants under one year of age, and two looked at its use as a booster in around 1,500 children. The studies looked at immunogenicity (the ability of the vaccine to make the immune system respond the bacteria and viruses that it contains) and safety.

How far into the evaluation was the application when it was withdrawn?
The application was at day 120 when the company withdrew. The CHMP had formulated a list of questions to be answered by the company, but the company had not yet responded to them.
The CHMP, in co-operation with the WHO, normally takes up to 210 days to evaluate a new application. Based on the review of the initial documentation, the CHMP prepares a list of questions at day 120, which is sent to the company. Once the company has supplied responses to the questions, the CHMP reviews them and may, before giving a scientific opinion, ask any remaining questions at day 180.

What was the recommendation of the CHMP at that time?
Based on the review of the data at the time of the withdrawal, the CHMP had some concerns and was of the provisional opinion that Globorix could not have received a positive scientific opinion.

What were the main concerns of the CHMP?
From the information presented by the company, it was not possible to establish the shelf life of the vaccine.
The vaccine was to be used in areas such as sub-Saharan Africa. The CHMP had concerns that there were too few children from this area in the studies to be able to see how effective it would be against meningitis and their response was apparently lower than that seen in children from other parts of the world. There was also insufficient information on the use of the vaccine as a booster.
Therefore, at the time of the withdrawal, the CHMP's view was that a benefit of Globorix had not been sufficiently demonstrated and any benefits did not outweigh the identified risks.

What were the reasons given by the company to withdraw the application?
The letter from the company notifying the EMEA of the withdrawal of the application is available here.

What are the consequences of the withdrawal for patients undergoing clinical trials with Globorix?
The company has informed the CHMP that there are no clinical trials currently running with Globorix.